UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

September 27, 1988

MEMORANDUM

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

SUBJECT: Mancozeb (014504)
Rohm and Haas Response to Registration Standard
Rohm and Haas letter of 6/8/88 (Response to EPA letter of 5/4/88
EPA Reg. No. 707-78
[No MRID No., RCB No. 4015]

FROM: Susan V. Hummel, Chemist
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Health Effects Division (TS-769C)

Susan V. Hummel

THRU: Edward Zager, Section Head
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Dietary Exposure Branch
Health Effects Division (TS-769C)

TO: Lois Rossi, PM #21
Herbicide Fungicide Branch
Registration Division (TS-767C)

Rohm and Haas has submitted a response to our memo of 4/21/88 (S. Hummel), which was forwarded to Rohm and Haas in EPA letter of 5/4/88. Rohm and Haas has responded to the EPA letter of 5/4/88 in their letter of 6/8/88.

Mancozeb is a coordination product of zinc ion and maneb (manganese zinc ethylenebisdithiocarbamate). Tolerances have been established for residues of mancozeb on a number of raw agricultural commodities including kidney and liver at 0.5 ppm (40 CFR 180.176). Tolerances for mancozeb are calculated as zineb equivalents. An interim tolerance for residues of mancozeb in potatoes is found in 40 CFR 180.319. Food and feed additive tolerances have been established for several processed commodities (21 CFR 193.460 and 21 CFR 561.410). One tolerance petition for residues of mancozeb in lettuce, peppers, and beans is in reject status (PP#3F2949, M. Kovacs, 12/10/87, RCB No. 2654).

The Product and Residue Chemistry chapters for the Mancozeb Registration Standard were completed on 9/10/86. An update was completed on 1/27/87. The Mancozeb Registration Standard (Guidance Package) was issued in April, 1987. EPA has also

announced the initiation of a Special Review of the ethylene bisdithiocarbamate pesticides (EBDCs), including mancozeb (52 FR 27172, 7/17/87).

CONCLUSIONS

1. Deficiency 1 regarding labeling remains outstanding.

2. Deficiency 2 regarding tolerance reassessment remains outstanding.

3a. The Rohm and Haas response to Deficiency 3a is under review. With regard to the tomato metabolism study in progress, we reiterate that the Registration Standard specifically states the need for sampling intervals through at least 21 days and that several sampling intervals are needed. Tomatoes should be initially sampled no later than five days after the last treatment, with additional sampling intervals up through at least 21 days after the last treatment.

3b. The Rohm and Haas response to Deficiency 3b is under review.

4a. Deficiency 4a regarding enforcement methodology capable of distinguishing between/among the different EBDC fungicides and degradates remains outstanding.

4b. The Rohm and Haas response to deficiency 4b is under review. See RCB Nos. 4265 and 4266.

5. Because of the differences in the results obtained by the various EBDC registrants, we have reconsidered our previous conclusion regarding storage stability data. We will require storage stability studies for EBDC's and ETU conducted concurrently with residue analyses for each crop group, for each growing season, and for each laboratory conducting residue studies.

   Storage stability samples fortified with mancozeb must be analyzed for mancozeb and ETU. Storage stability samples fortified with ETU must be analyzed for ETU. The Registration Standard deficiency for storage stability data is outstanding. Because of differences between laboratories, we will not accept storage stability data from one laboratory to support residue data from another laboratory.

   Our comments on the Rohm and Haas Storage Stability Protocols are found in S. Hummel memo of 9/8/88.

6. Deficiency 6 regarding Residue and Processing data remains outstanding.

We reiterate our previous conclusion regarding the support of dust formulations. We have no objection to the deletion of residue data for the dust formulations, provided that all dust formulations of mancozeb are cancelled, including use directions on the Dithane M-45 (707-102) label for formulating dust formulations.

6a. Deficiency 6a remains outstanding. An insufficient number of side by side field trials were conducted. In order to conclude that residues from ground and aerial trials are comparable, side by side field trials are needed as discussed above for carrots, celery, and sweet corn, as well as side by side field trials for one crop in each crop group not represented by carrots, celery, or sweet corn.

The registrant should also be reminded that the full range of types of applications should be represented, including all spray volumes which are registered (dilute, concentrate, and ULV, if applicable).

RECOMMENDATIONS

We recommend that the registrant be informed of our conclusions and be advised to resolve the Registration Standard deficiencies. We recommend that the registrant receive this review in its entirety. We continue to recommend that the registrant be informed of Deficiency 4a in 3(c)2(B) format.

Rohm and Haas response to data gaps

Deficiency 1 - Labeling

The registrant must propose a maximum number of applications per season or a maximum seasonal rate for each crop. The submitted residue data must reflect this proposed maximum rate.

Registrant Response

No revised labeling was included in this submission. Rohm and Haas indicates that they will propose labeling changes when they submit the required residue data in October, 1988.

DEB Comment

This deficiency remains outstanding. Additional labeling changes may be required when the required residue data are submitted and reviewed.

Deficiency 2 - Tolerance Reassessment

Data gaps exist for plant and animal metabolism and storage stability. Thus any conclusions made at this time regarding the adequacy of existing tolerances are subject to change. Tolerances for animal commodities will not be assessed until the requested animal metabolism studies are completed and reviewed.

Established tolerances for residues of mancozeb in/on wheat, barley, oat, and rye processed products are tentatively considered adequate, but will be reassessed when residue data on wheat are submitted.

Insufficient data are available to ascertain the adequacy of the established tolerances for residues of mancozeb in/on apples, asparagus, bananas, carrots, celery, corn (fresh), corn fodder and forage, corn grain, cottonseed, cranberries, cucumbers, grapes, melons, onions, papayas, peanuts, peanut vines and hay, pears, potatoes, sugar beet roots and tops, summer squash, tomatoes, wheat grain, and wheat straw.

Although insufficient data are available to ascertain the adequacy of established tolerances for residues of mancozeb in/on barley grain and straw, crabapples, oat grain and straw, quinces, and rye grain and straw, no residue data are required for these commodities, since the necessary residue data will be translated from the crops listed in the previous paragraph.

Processing studies are required for corn, cottonseed, peanuts, potatoes, and sugar beets. Tolerances may be required for processed commodities of these racs.

Tolerance proposals and residue data are required for barley forage, barley hay, corn silage, oat forage, oat hay, peanut hulls, rye forage, wheat forage, and wheat hay. Alternatively, feeding restrictions may be proposed for all these except corn silage and peanut hulls.

Food/feed additive tolerances must be proposed for dry apple pomace, grape pomace (wet and dry), grape juice, and raisin waste.

Tolerance proposals and/or residue data are required reflecting seed or propagation stock treatment of flax, pineapple, rice, safflower, and sorghum.

Registrant Response

None. No tolerance proposals were included in this submission.

DEB Comment

This deficiency remains outstanding.

Deficiency 3a - Nature of the Residue - Plants

Data depicting the uptake, distribution, and metabolism of mancozeb in pome fruit and fruiting vegetable crops following foliar applications must be submitted. Sampling intervals through at least 21 days must be included. The identities and quantities of residues in or on mature plant parts must be determined in order to elucidate the terminal residues. Residue identities must be confirmed by a method such as GC, HPLC and/or mass spectroscopy. Data reflecting solvent extraction efficiency of mancozeb residues must also be presented. Representative samples from these tests must also be analyzed by enforcement methods to ascertain that these methods are capable of determining all metabolites of concern.

(From text of Residue Chemistry Chapter and addendum, not in Registration Standard Tables.) The metabolism of mancozeb is adequately understood for soybeans, but not for wheat. Over 70% of the 14C activity in soybeans was characterized, and almost 100 % of the activity in soybean pods was characterized. The sugar beet metabolism study was adequate for sugar beet roots, because 59% of the activity in roots was characterized as either EBDC metabolites or natural products. However, only 32% of the activity in sugar beet tops was characterized.

DEB Comment (from S. Hummel memo of 4/21/88)

The additional information submitted by Rohm and Haas is under review. However, even if the metabolism studies on sugar beet tops and wheat are considered to be valid studies, additional metabolism data will be needed on tomatoes and possibly apples. Although not specifically stated in the Registration Standard, metabolism studies on a pome fruit and on a fruiting vegetable crop were needed because of the large amount of mancozeb use on these types of crops. The three crops chosen by Rohm and Haas for metabolism studies each account for less than 2 % of mancozeb use. Additionally, wheat and soybean samples were not taken at short enough intervals after the final treatment to be considered representative of the use on apples and tomatoes. The first wheat and soybean samples were taken

over 45 days after the last treatment. The Registration Standard specifically states the need for sampling intervals through at least 21 days. Several sampling intervals are needed. Tomatoes should be initially sampled no later than five days after the last treatment, with additional sampling intervals up to at least 21 days after the last treatment.

Thus, a waiver from the requirement of additional metabolism data on apples and tomatoes is not justified. The requirement for additional metabolism data on apples may be waived if the metabolism of mancozeb on tomatoes is similar to the metabolism of mancozeb on other crops. This deficiency remains outstanding. Review of the additional information submitted by the registrant regarding the sugar beet and wheat metabolism studies will continue.

Registrant Response to EPA letter of 5/4/88

In their letter of 6/8/88, Rohm and Haas stated that they would conduct a plant metabolism study on tomatoes with samples taken at the label PHI of 5 days.

DEB Comment

We reiterate that the Registration Standard specifically states the need for sampling intervals through at least 21 days and that several sampling intervals are needed. Tomatoes should be initially sampled no later than five days after the last treatment, with additional sampling intervals up through at least 21 days after the last treatment.

This deficiency remains outstanding.

Deficiency 3b - Nature of the Residue - livestock

> Metabolism studies utilizing poultry are required. Animals must be dosed for three days with [14C] mancozeb at a level sufficient to make residue identification and quantification possible. Eggs must be collected twice daily during the dosing period. Animals must be sacrificed within 24 hours of the final dose. The distribution and characterization of residues must be determined in eggs, liver, kidney, muscle, and fat. Precautions must be taken to minimize EBDC degradation during analysis steps due to the presence of water, methanol, and atmospheric oxygen. Samples from the studies requested above should also be analyzed using current enforcement methods to ascertain the validity of these methods. Upon receipt of the requested data, the need for, and nature of, tolerances for residues in animal products will be determined.

Registrant Response

Rohm and Haas submitted a letter clarifying previously submitted studies.

DEB Comment

The additional information submitted by Rohm and Haas is under review.

Deficiency 4 - Residue Analytical Method

Deficiency 4a - Enforcement Analytical Method

(This requirement was listed in the text, but not in the tables. It should be sent to the registrant in 3(c)2(B) format.

An enforcement method is needed which is capable of distinguishing between/among the different EBDC fungicides.

Registrant Response

Rohm and Haas requested a waiver from the requirement of enforcement methodology which distinguishes between the different EBDC pesticides. They state that the current method measures CS_2 evolution and applies to all EBDC fungicides. The EBDC fungicides differ chemically only by the metal cation associated with the ethylenebisdithiocarbamate moiety. A specific method would require specific analysis based on the metal cations, which also occur naturally in the crop matrix. It is not possible to distinguish metal cations due to residues from naturally occurring metals. Therefore, this requirement should be waived.

DEB Comment (from S. Hummel memo of 4/21/88)

A waiver of the requirement for enforcement methodology which distinguishes between the different EBDC fungicides is not appropriate. The Agency needs to be able to distinguish between the different EBDC fungicides for enforcement purposes. While analysis for the metal cations may not distinguish mancozeb residues from other EBDC residues or from naturally occurring metal cations, other types of analysis may be possible. Additionally, an enforcement method is needed to distinguish between/among other contaminants which degrade to CS_2.

Registrant Response

Rohm and Haas would like to meet with EPA to discuss analytical methods.

DEB Comment

We reiterate our previous comment form S. Hummel memo of 4/21/88.

Deficiency 4b - Multiresidue Methodology

Residues of ethylenethiourea (ETU) and mancozeb, per se, in/on crop samples must be subjected to analysis by the multiresidue methods published as an addendum to Subdivision O. Protocols for methods I, II, III, and IV are available from NTIS under Order No. PB86 203734/AS.

Registrant Response

Rohm and Haas indicates that they are currently testing mancozeb and ETU through the PAM I methods and will submit data by July, 1988. These data have recently been received and are under review. (RCB# 4265, 4266)

DEB Comment

We reserve comment until the review of these data is complete.

Deficiency 4c - Analytical Methodology - Additional metabolites

If the requested data regarding the nature of the residue in plants and animals reveal additional metabolites of toxicological concern, additional analytical methods for data collection and enforcement may be required.

Registrant Response

None.

DEB Comment

No response is needed from the registrant at this time.

Deficiency 5 - Storage Stability

Available storage stability data are adequate to demonstrate that mancozeb is stable in/on frozen plant samples for up to 12 months and ETU is stable for up to 6 months in frozen plant samples.

To support crop residue data, storage stability studies must be conducted on both weathered samples (mancozeb) and fortified frozen samples (mancozeb, metabolites and ETU) of one representative crop from

each crop grouping (40 CFR 180.34) on which registered uses of mancozeb exist. Analyses of each crop must be conducted over a time period that includes the time interval that the raw agricultural commodity is held in frozen storage prior to the crop residue analysis. To support residue data on processed commodities, fortified storage stability data are required for all processing studies submitted to the Agency. Analyses must be conducted over a time period that includes the frozen storage of the raw agricultural commodity prior to processing and each processed commodity prior to the residue analysis. Protocols for these studies must be submitted to and approved by the Agency prior to initiating the studies.

(a) Storage stability data using weathered samples. Data are required on the parent compound, mancozeb, in which crop samples field treated with a typical end use product are frozen immediately upon harvesting. The integrity of the samples must be maintained by freezing. The samples must be analyzed for mancozeb on the day they arrive at the analytical laboratory, and then stored frozen and analyzed periodically for mancozeb during the time intervals specified in the Agency approved protocol.

(b) Storage stability data using fortified samples. Data are required on mancozeb, ETU, and metabolites in which a group of untreated samples of raw agricultural commodities and processed crops are fortified (spiked) with only mancozeb pure active ingredient, another group of samples is fortified with only ETU, and other groups are fortified individually with each additional metabolite. Immediately after fortification, the samples fortified with mancozeb must be analyzed for mancozeb and ETU; samples fortified with ETU must be analyzed for only ETU; and samples fortified with other metabolites must be analyzed for only the metabolite with which the sample was fortified. Sample integrity must be maintained by freezing, and analyses for mancozeb, ETU, and metabolites must be conducted periodically during the time intervals specified in the Agency approved protocol.

(c) Storage stability data for livestock/poultry feeding studies. If cattle and poultry feeding studies are required (see Registration Standard Guidance Package, Data Table footnotes 71 and 72), fortified storage stability studies will be required on all animal commodities (i.e., tissues, milk and eggs) for which residue data are submitted to the Agency. Analyses must be conducted over a time period that

includes the time interval that each commodity is held in frozen storage prior to residue analyses.

(These deficiencies were in the text and not in the Guidance Package Table Footnotes.)

All requested residue data must be accompanied by data regarding storage intervals and conditions of sample storage from harvest until analysis.

If metabolism studies reveal the presence of other metabolites of concern, then storage stability studies must be conducted on these additional metabolites for the length of time the samples were stored.

Registrant Response

Rohm and Haas claims that the storage stability studies they have submitted are adequate. They claim that weathered residue storage stability studies are not needed. Rohm and Haas states that they will provide harvest to analysis intervals for each crop analysis, along with sample storage conditions.

Fortified storage stability protocols for livestock and poultry tissues and crop samples have recently been submitted. (See DEB No. 3202.)

DEB Comment from S. Hummel memo of 4/21/88

The registrant is correct in stating that the fortified storage stability studies they have submitted are adequate to show that mancozeb is stable in frozen storage for up to 12 months and that ETU is stable in frozen storage for up to 6 months. However, storage intervals and conditions of sample storage from harvest until analysis were not available for the residue data reviewed for the Registration Standard. Thus, any data submitted for which the frozen storage interval is longer than 12 or 6 months for mancozeb or ETU, respectively, are not valid.

Weathered storage stability studies will not be required if all samples were analyzed within 12 months of harvest for mancozeb and within 6 months for ETU, and were stored frozen from harvest until analysis. If any samples were stored longer than 12 months and 6 months, then both weathered and fortified storage stability data are needed.

DEB Comments (from S. Hummel memo of 9/8/88)

Because of the differences in the results obtained by the various EBDC registrants, we have reconsidered our previous conclusion regarding storage stability data. We will require

storage stability studies for EBDC's and ETU conducted concurrently with residue analyses for each crop group, for each growing season, and for each laboratory conducting residue studies.

Storage stability samples fortified with mancozeb must be analyzed for mancozeb and ETU. Storage stability samples fortified with ETU must be analyzed for ETU. The Registration Standard deficiency for storage stability data is outstanding. Because of differences between laboratories, we will not accept storage stability data from one laboratory to support residue data from another laboratory.

Comments on Storage Stability Protocols (from S. Hummel memo of 9/8/88)

a. Test Materials and Spiking Solution: The Registration Standard specifically requires that the study be conducted using the pure active ingredient (PAI), not a formulated product (Dithane M-45).

b. Testing Facility: The use of Enviro-Bio-Tech to conduct the storage stability study is acceptable, provided that Enviro-Bio-Tech also conducts all analyses of crop field trial samples and animal feeding study samples. We will not accept storage stability data from one laboratory to support residue data from another laboratory.

c. Samples to be analyzed: The samples to be analyzed should be one sample from each crop group for which mancozeb is registered. The choice of samples for animal commodities are acceptable.

d. Preparation and analysis of crop samples: The storage stability samples should be handled in exactly the same manner as the field trial or feeding study samples. The use of whole crop samples is acceptable, provided this is how the crop field trial samples are handled. The registrant should be cautioned that it is extremely difficult to uniformly spike whole samples. The partial thawing, homogenizing, and refreezing of storage stability samples 24 hours before analysis would also be acceptable, provided this is how the field trial samples are handled.

3. The registrant should also consult the OPP Position Document on Storage Stability for further information.

Deficiency 6- Residue and Processing Data

Detailed deficiencies will not be listed here. These deficiencies list treatment rates and number of treatments, and required geographical representation for wettable powder and dust formulations. Ground vs. aerial applications are discussed below.

Registrant Response

Rohm and Haas will conduct additional trials with the 80WP formulation, but will not conduct residue trials with the dust formulation.

DEB Comment (from S. Hummel memo of 4/21/88)

We have no objection to Rohm and Haas not supporting the dust formulations, providing all registrations for dust formulations of mancozeb are cancelled. Ground vs. aerial applications are discussed below.

Rohm and Haas Response to EPA letter of 5/4/88

Rohm and Haas has no registrations for dust formulations. However, Dithane M-45 Concentrate (EPA Reg No. 707-102) is an MUP, which some registrants use to formulate dust formulations.

DEB Comment

We reiterate our previous comment that we have no objection to the deletion of residue data for the dust formulations, provided that all dust formulations of mancozeb are cancelled, including use directions on the Dithane M-45 (707-102) label for formulating dust formulations.

Ground vs. Aerial Applications

Residue data comparing ground and aerial applications are required.

DEB Comment (from S. Hummel 4/21/88 memo)

The summary table submitted to compare ground and aerial applications does not clearly state from which study each data point was obtained, and therefore cannot be further evaluated. However, all previously submitted data were reviewed for the Registration Standard and the requirement for both ground and aerial data was made after considering all previously submitted data. We reiterate that residue data are needed for both ground and aerial applications. The registrant might consider conducting a bridging study to satisfy this requirement. A bridging study would involve side by side residue field trials

for at least one crop in each crop group. Separate side by side tests would be needed for several diverse locations for each crop.

Registrant response to EPA letter of 5/4/88

Rohm and Haas resubmitted the summary table of previously submitted data which was submitted as part of the Rohm and Haas 90 day Response. The registrant stated that residue levels were similar for both types of applications, and therefore, only one type of application should be sufficient for future residue field trials.

Discussion of Data

Asparagus (MRID No. 00160715). One aerial trial. No ground and aerial trials were side by side; none were the same application rate and PHI.

Barley (MRID No. 00160717). Four aerial trials. No ground trials. No side by side ground and aerial trials.

Carrots (MRID No. 00160707, Accession No. 261540). Two aerial trials. One side by side trial with same rate and PHI in Gonzolas, CA. Similar residues were reported, with the exception of one data point.

Celery (MRID No. 00160718, Accession No. 261999). Five aerial trials; four in Salines, CA. One side by side trial with same rate and PHI in Salines, CA. Similar residues were reported in ground and aerial trials in Salines, CA.

Corn, field (MRID No. 00160719). Five aerial trials. No side by side trials using same rate, same PHI, and sampling the same plant parts.

Corn, sweet (MRID No. 00160720, Accession No. 262000). Two aerial trials. One pair of trials at same rate and PHI were reasonably close to each other - one in LeSueur, MN, north of Mankato on US 169; and one in Waseca, MN, east of Mankato on US 14. Similar residues were reported in this pair of trials.

Onions (MRID No. 00160723). One aerial trial. No side by side trials.

Sugar Beets (MRID No. 00160726, Accession No. 262003). Four aerial trials. Two aerial trials were identified in the summary sheet as being in MN, but the raw data sheets identify the location as Casselton, ND, 20 mi west of Moorhead, MN. One ground trial in Moorhead, MN. This pair of trials were not at the same total application rate (different numbers of trials) and not all at the same PHI. Similar residues were reported at 7-14

day PHIs. A pair of trials were conducted in Salines, CA; however, one trial used both ground and aerial application.

DEB Comment

Carrots Side by side trials were conducted in CA. Additional side by side trials are needed from TX and NY.

Celery Side by side trials were conducted in CA. Additional side by side trials are needed in FL and MI.

Corn, sweet Side by side trials were conducted in MN. Additional side by side trials are needed from FL and WA/OR.

Sugar Beets No side by side trials were conducted.

An insufficient number of side by side field trials were conducted. In order to conclude that residues from ground and aerial trials are comparable, side by side field trials are needed as discussed above for carrots, celery, and sweet corn, as well as side by side field trials for one crop in each crop group not represented by carrots, celery, or sweet corn.

The deficiency for ground and aerial residue data remains outstanding. The registrant should also be reminded that the full range of types of applications should be represented, including all spray volumes which are registered (dilute, concentrate, and ULV, if applicable).

cc:R.F., circu, S. Hummel, mancozeb S.R.F. (Hummel), mancozeb R.S.F. (Boodee), mancozeb S.F., V. Bael (SRB/RD), TOX, PMSD/ISB
RDI:EZ:09/26/88:RDS:09/26/88
TS-769:DEB:SVH:svh:RM810:CM#2:x77324:9/27/88